Antimicrobial Agents And Chemotherapy
Volume 48, Issue 10 , October 2004, Pages 3975-3979
ISSN: 0066-4804

MEDLINE®

Rifalazil treats and prevents relapse of clostridium difficile-associated diarrhea in hamsters

Anton, Pauline M; O'Brien, Michael; Kokkotou, Efi; Eisenstein, Barry; Michaelis, Arthur; Rothstein, David; Paraschos, Sophia; Kelly, Ciáran P; Pothoulakis, Charalabos

Beth Israel Deaconess Medical Center, Division of Gastroenterology, Dana 601, 330 Brookline Ave., Boston, MA 02215, USA; e-mail cpothoul@bidmc.harvard.edu

Abstract

Although vancomycin and metronidazole effectively treat Clostridium **difficile**-associated diarrhea and colitis (CDAD), their use is associated with a high incidence of relapsing C. **difficile** infection. Rifalazil is a new benzoxazinorifamycin that possesses activity against Mycobacterium tuberculosis and gram-positive bacteria. Here we compared rifalazil and vancomycin for effectiveness in preventing or treating clindamycin-induced cecitis in a hamster model of CDAD. Golden Syrian hamsters were injected subcutaneously with clindamycin phosphate (10 mg/kg), followed 24 h later by C. **difficile** gavage. Hamsters received by gavage for 5 days vehicle, vancomycin (50 mg/kg), or rifalazil (20 mg/kg) either simultaneously with (**prophylactic protocol**) or 24 h after C. **difficile** administration (treatment protocol). While all vehicle-administered animals became moribund within 48 h of C. **difficile** administration, no rifalazil- or vancomycin-treated animals in either protocol showed signs of morbidity after 7 days. Ceca of rifalazil-treated animals showed absence of epithelial cell damage, significantly reduced congestion and edema, and less, but not statistically significantly less, neutrophil infiltration compared to those of vehicle-treated animals. In contrast, vancomycin-treated animals demonstrated severe epithelial cell damage and mildly reduced congestion and edema. Moreover, hamsters relapsed and tested C. **difficile** toxin positive (by enzyme-linked immunosorbent assay) 10 to 15 days after discontinuation of vancomycin treatment. None of the rifalazil-treated hamsters showed signs of disease or presence of toxins in their feces 30 days after discontinuation of treatment. Our results indicate that once daily rifalazil may be superior to vancomycin for curative treatment

of CDAD. [Journal Article; In English; United States]

CAS Registry Numbers: Anti-Bacterial Agents; Rifamycins; 129791-92-0, KRM 1648; 1404-90-6, Vancomycin

Citation Subset Indicators: Index Medicus

MeSH Terms: Animals; Anti-Bacterial Agents, * pharmacology (PD), * therapeutic use (TU); Cecum, drug effects (DE), microbiology (MI); Clostridium ‹difficile›, * drug effects (DE); Comparative Study; Diarrhea, * drug therapy (DT), microbiology (MI); Enterocolitis, Pseudomembranous, * drug therapy (DT), prevention & control (PC); Enzyme-Linked Immunosorbent Assay; Hamsters; Mesocricetus; Microbial Sensitivity Tests; Recurrence, prevention & control (PC); Research Support, Non-U.S. Gov't; Rifamycins, pharmacology (PD), * therapeutic use (TU); Survival Analysis; Vancomycin, pharmacology (PD), therapeutic use (TU); Weight Loss, drug effects (DE)

Antimicrobial Agents And Chemotherapy
Volume 48, Issue 10 , October 2004, Pages 3975-3979
ISSN: 0066-4804